



#### REMS RISKS

## FDA's Woodcock On FDAAA

MAY 27, 2008

---

- Last week, we quoted Wyeth's Joseph Camardo on the renewed user fee legislation known as FDAAA. He's not sure the new post-marketing environment is starkly different from the old one. In thinking of the still-murky FDAAA regulatory landscape, we were reminded of a lyric from The Who: "Meet the new boss, same as the old boss."

Janet Woodcock, head of the FDA **Center for Drug Evaluation and Research (CDER)**, is in the unusual position of being *both* the new boss and the old boss. Simultaneously.

### Prickly Situation

So when Woodcock took the podium at the Post-Approval Summit at Harvard two weeks ago, she was in a delicate spot. She couldn't appear at the **Outcome**-organized conference and say that last autumn's FDAAA legislation was merely going to perpetuate what the agency has always done. That might displease Einstein-like politicians who finally seem to grasp that they had underfunded the FDA for a decade.

Yet neither could Woodcock overstate the likely impact of FDAAA, since the user-fee legislation doesn't really give industry any significant new burdens or requirements. The pre-Vioxx system—in which industry and FDA negotiate additional trials after a drug has been approved—remains intact.

To be fair, FDAAA does grant the FDA a few limited powers that the public assumed it should have had all along—mainly around a bit more control of the clock during drug safety controversies.

Woodcock's strategy was to forcefully point out what will change around the margins. Of FDAAA, she said, "It's a response by Congress to what they saw as FDA's weaknesses. Some of this will be dry. But it's really important. It's going to change the landscape in the future."

### 15-Day Deadlines

FDAAA, Woodcock noted, now allows the FDA to demand additional post-approval trials, but only under circumscribed circumstances. “We have to make a finding that the study is really needed because we can’t find the information out in other ways,” she notes. “We can’t just arbitrarily call for new studies.”

In theory, there could be a 15-day timer that the FDA can set when it feels sponsors are not adjusting a drug’s label with sufficient urgency. Again, however, Woodcock noted the Congressionally-imposed limits on the agency’s latitude: “But—here again—are the caveats. The sponsor can appeal this.”

A key element in the new landscape is a risk evaluation and management strategy (REMS). That plan may be due 120 days after an FDA request, although that deadline too can be negotiated. A REMS, it should be noted, can widely range in scope and complexity, and could significantly restrict patient access to some drugs. The agency has been issuing a few REMS letters already, Woodcock says.

### **Putting it in the Statute**

The REMS is a cousin of a risk management plan (or RiskMAP), and Woodcock was careful to say that the change in the law is incremental. “Before a drug is approved, FDA may determine a REMS is needed. We have been doing this all along. We invented the concept of risk management as it applied to pharmaceuticals. But this was not in the statute. Now this is codified in the statute.”

What’s the change? The agency can remove a drug from the market on its own. “This type of authority is new,” says Woodcock. In the past, Woodcock said, such deliberations “have been a negotiation. They have not been backed up by statutory authority.”

### **REMS Risks**

But it’s clear that Woodcock is aware of the paperwork and procedural burdens that might be incorporated into the most involved risk-mitigation efforts that involve physicians, pharmacists, and laboratories working together, as is the case with drugs like Accutane or Thalidomide, to ensure no patients receive a drug inappropriately.

Rolling out such REMS too broadly across a limping, disconnected U.S. health care system, she says, is probably not a wise move. Said Woodcock: “It puts a huge burden on the health care system, which is not very functional as we all know. It will probably cause more errors rather than prevent them.” We took that to mean that the FDA will demand the most complex REMS sparingly.

### **New Safety System**

In some cases, she said, sponsors that have not fulfilled their responsibilities under the law will have limited options: “We can withdraw the drug without first ordering the assessment”

of a REMS or RiskMAP, Woodcock said. Noting the \$250,000 per violation penalties, she added: “There’s teeth to all this.”

In addressing the systems and tools that the FDA will be developing to do its own analysis of drug safety, she conceded the post-Vioxx environment will be challenging. “Figuring out how to analyze the data is going to be our problem. It’s going to be harder than one might think.”

### **‘What the Public Expects’**

Woodcock said the initial budget of \$25 million for a new drug safety surveillance system would be only a down payment, and candidly addressed the difficulties ahead. “We need a new system which we are in the process of trying to purchase,” she said. “This will be difficult to do until we have better analytic tools. This is scientifically and operationally challenging, but this is what the public expects us to do.”

One concept is “active surveillance.” It’s years away, if it ever can be done. But the FDA is planning to use commercial databases, other federal databases, and a bit of IT magic to get its own glimpse of safety signals before or in concert with what industry tells it. We thus foresee an analytic arms race of sorts, in which industry spends a little money to make sure it can see safety signals before regulators.

“Congress is envisioning something broader and much more active—sort of an artificial intelligence system,” Woodcock noted. (Our mood always brightens upon hearing “intelligence” and “Congress” in the same sentence.)

### **See You In Court**

But then Woodcock nudged us back to reality. She said that the final chapter of FDAAA would probably be written in the courts, not by the agency itself. “There are going to be lawsuits and litigation around this statute,” she said. “There will be pieces that will be litigated.”

The bottom line, in the end, is that FDAAA places no significant new requirements on industry. Product withdrawals will still be negotiated. The time lines for post-approval trials will still be worked out in a cordial, gentlemanly fashion.

Yes, FDAAA does give the FDA new authority that will be used in rare circumstances. No doubt one or two sponsors with impaired hearing will suddenly find themselves under the searing pressure of the 15-day clock. (A few such instances will encourage better listening throughout the industry.) But most sponsors, most of the time, will be able to design post-marketing trials as they always have.

Editor’s note: people who want to read [the FDAAA statute](#) can find it here.